REMARKS

Claims 2-11 and 37-39 are pending in the application. Claims 2 and 3 have been amended to better describe the claimed invention, and thus for reasons unrelated to patentability. Support for the amendment is found throughout the Specification, for example, at page 39, lines 11-15 ("The difference between the consensus ORF sequence of HC-J6$_{CH}$ from the experimentally infected chimpanzee and that of HC-J6 of the inoculum (Okamoto et al., 1991) was **4.1%** and **2.2%** at the nucleotide and deduced amino acid levels, respectively (Fig. 2, Table 2).") See also Table 2 at page 40 showing that the percent difference of nucleotide sequences between strain HC-J6 (Okamoto et al., 1991) and strain HC-J6$_{CH}$ **as measured from nucleotide position 341-9439, which corresponds to the ORF**, is **4.1% at the nucleotide level** and the percent difference of predicted amino acid sequence between strain HC-J6 (Okamoto et al., 1991) and strain HC-J6$_{CH}$ is **2.2% at the amino acid level**. No new matter is being added herewith.

I. Compliance with 35 USC 102/103

The Patent Office rejected the claims under 35 USC 102(b) as anticipated by Okamoto et al. 1991 J. Gen. Virol. 72: 2697 in light of Doorn et al. 1995 J. Gen. Virol. 76: 1871 (see Fig. 1 on page 1873) or, in the alternative, under 35 USC 103(a) as obvious over Okamoto et al. 1991 J. Gen. Virol. 72: 2697 and further in view of Yoo et al. 1995 J. Virol. 69: 32.

Under new grounds for rejections, the Patent Office rejected the claims under 35 USC 102(b) as anticipated by Okamoto et al. (EP 532 167 A2).

Additionally, under new grounds for rejection, the Patent Office rejected the claims under 35 USC 102(b) as anticipated by Okamoto et al. (USP 5,428,145).

Furthermore, under new grounds for rejection, the Patent Office rejected the claims under 35 USC 103(a) as unpatentable over Okamoto et al. (USP 5,428,145) and further in view of Yoo et al. 1995 J. Virol. 69: 32.

Claims 3 and 38-39 are deemed by the Patent Office free of art. The claims must be patentable over the prior art. The references do not constitute patentability-defeating prior art.

Starting with the general state of the art, according to Yanagi et al., 1999 Virology 262: 250, at p. 250, ¶ bridging col. 1 & 2, of record, HCV is a virus that has a positive-sense single-strand RNA genome approximately 9.6 kb in length. The single long open reading frame (ORF), which encodes a polyprotein, is flanked by 5' and 3' untranslated regions (UTRs). The 5' UTR contains an

internal ribosome entry site (IRES). The 3' UTR consists of 3 regions: a short variable region, a polypyrimidine tract of variable length, and a highly conserved terminal region of approximately 100 nts. The polypyrimidine tract and the conserved region of the 3' UTR are essential for infectivity in vivo.

Turning to the references, Okamoto et al. (1991 J. Gen. Virol. 72: 2697), Okamoto et al. (EP 532 167 A2), and Okamoto et al. (USP 5,428,145), all describe the cDNA of the isolate HC-J6 but do not describe the highly conserved terminal region of approximately 100 nts essential for infectivity in vivo. Doorn et al. classifies HC-J6 as genotype 2a (see Fig. 1 on page 1873). Rice et al. (no longer cited as prior art) describes the highly conserved terminal region of approximately 100 nts that turns out to be essential for infectivity in vivo. Yoo et al. describes transfection of a differentiated human hepatoma cell line with in vitro-transcribed HCV RNA that lacks the polypyrimidine tract and the highly conserved terminal region of approximately 100 nts essential for infectivity in vivo (see p. 33, col. 2, "results," and FIG. 1), thus infectivity in vivo would be prevented and any perceived infectivity in vitro was probably an artifact. The references, whether taken singularly or together, neither teach nor suggest the claimed invention.

The claims as amended are directed to:

> 2. A purified and isolated nucleic acid molecule which encodes human hepatitis C virus of genotype 2a, said molecule capable of expressing said virus when transfected into cells and further capable of infectivity in vivo, wherein said molecule encodes the amino acid sequence of SEQ ID NO: 2 or encodes an amino acid sequence that differs from that of SEQ ID NO: 2 by < 2.2% at the amino acid level.

or:

> 3. The nucleic acid molecule of claim 2, wherein said molecule comprises the nucleic acid sequence of SEQ ID NO: 1 or comprises a nucleic acid sequence that differs from that of SEQ ID NO: 1 from nucleotide 341 to 9439, which corresponds to the ORF, by < 4.1% at the nucleotide level.

Attached is Declaration under 37 CFR 1.132 of Raymond Smith, Ph.D. Dr. Smith is a patent agent representing Applicant and a molecular biologist. Dr. Smith compared the percent

difference of nucleotide sequences between strain HC-J6 (Okamoto et al., 1991) and strain HC-$J6_{CH}$ **as measured from nucleotide position 341-9439, which corresponds to the ORF**, and the percent difference of predicted amino acid sequence between strain HC-J6 (Okamoto et al., 1991) and strain HC-$J6_{CH}$. Dr. Smith determined that the percent identity of nucleotide sequences between strain HC-J6 (Okamoto et al., 1991) and strain HC-$J6_{CH}$ **as measured from nucleotide position 341-9439, which corresponds to the ORF**, is **95.9% at the nucleotide level** and the percent identity of predicted amino acid sequence between strain HC-J6 (Okamoto et al., 1991) and strain HC-$J6_{CH}$ is **97.8% at the amino acid level**. Thus, the evidence shows that the percent difference of nucleotide sequences between strain HC-J6 (Okamoto et al., 1991) and strain HC-$J6_{CH}$ **as measured from nucleotide position 341-9439, which corresponds to the ORF**, is **4.1% at the nucleotide level** and the percent difference of predicted amino acid sequence between strain HC-J6 (Okamoto et al., 1991) and strain HC-$J6_{CH}$ is **2.2% at the amino acid level.**

For these reasons, the references, whether taken singularly or together, neither teach nor suggest the claimed invention, and thus the rejections under 35 USC 102/103 should be withdrawn.

CONCLUSION

In view of the above, it is submitted that the claims are in condition for allowance. Reconsideration and withdrawal of all outstanding rejections are respectfully requested. Allowance of the claims at an early date is solicited. If any points remain that can be resolved by telephone, the Examiner is invited to contact the undersigned at the below-given telephone number.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 12/22/04

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